IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellant:	Jacobus M. Lemmens et al.
Title:	***Paroxetine Compositions and Processes for Making the Same***
Appl. No.:	10/678,082
Filing Date:	10/6/2003
Examiner:	Chris E. SIMMONS
Art Unit:	1612
Confirmation Number:	4414

PRE-APPEAL BRIEF REQUEST FOR REVIEW

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This Pre-Appeal Brief Request For Review is being filed together with a Notice of Appeal.

REMARKS

A Final Office Action dated May 11, 2010 maintained just a single rejection of pending claims 51-59 under 35 U.S.C. § 103(a) for being allegedly unpatentable over U.S. Patent No. 6,113,944 to Pathak *et al.* ("Pathak") in view of U.S. Patents No. 5,874,447 to Benneker *et al.* ("Benneker") and No. 4,675,188 to Chu. Because the rejection embodies clear legal and factual error, Appellants respectfully urge its withdrawal.

As reflected in independent claims 51 and 56, the claims on appeal are directed to pharmaceutical compositions comprising a sulfonate salt of paroxetine, calcium hydrogen phosphate anhydrate in the form of plate shaped crystals or agglomerates thereof, a disintegrant and a lubricant, wherein the composition does not contain lactose or microcrystalline cellulose, and wherein the composition has a pH within the range of 5.0 to 6.0.

The Action cited Pathak for alleged disclosure of paroxetine formulations with excipients such as calcium phosphate, sodium starch glycolate and magnesium stearate. As recognized by the Action, Pathak does not teach or suggest the use of a sulfonate salt of paroxetine or calcium hydrogen phosphate anhydrate in the form of plate shaped crystals or agglomerates. Moreover, Pathak does not teach or suggest that the paroxetine formulations should have a pH of 5.0 to 6.0.

The Action relied upon Benneker for teaching sulfonate salts of paroxetine. Further, the Action cited Benneker for alleged suggestion that such salts exhibit greater solubility.

The Action cited Chu for teaching the use of calcium hydrogen phosphate anhydrate ("CHP") for direct compression tableting. Critical to the stated rejection, the Action relied upon Chu also for its teachings regarding pH, as discussed in more detail below.

The rejection hinges upon at least two errors. First, the Action contended that the "prior art suggest[s] a composition that is substantially identical to that which is claimed . . ." and, hence, the prior art compositions would "reasonably be considered" to possess the claimed pH of 5.0 to 6.0.[1]

Second, the Action asserted that because Chu teaches a pH of the ***reaction medium*** in which calcium hydrogen phosphate ("CHP") can be prepared, then the ***final product***, CHP, "is reasonably considered to maintain a similar – if not the same – pH ***when mixed with the active ingredients*** to form the tablet,"[2] even though ***no scientific theory*** supports this extrapolation of pH of a ***component***, CHP, to pH of a ***composition*** containing that component. The Action cited Chu's teaching that adjustment of pH of the ***reactions*** producing CHP can affect "the shape and size of [CHP] particles," by identifying pH as a parameter suitable for optimizing.[3] From this, the Action concluded that "the pH [of the claimed composition] is still reasonably considered to be the same."[4]

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[1] Final Office Action dated May 11, 2010 at page 3; *see also* Interview Summary dated October 13, 2009.

[2] Final Office Action, page 4

[3] Final Office Action, page 3

[4] Final Office Action, page 4

I. Chu Does Not Suggest pH of a Composition that Contains Calcium Hydrogen Phosphate

The rejection is founded on factual error in that the only pH discussed by Chu is that of a ***reaction medium*** from which its anhydrous dicalcium phosphate is ultimately isolated.[5] Chu does not teach the pH of any resulting CHP product nor does the reference hint at pH of a pharmaceutical composition that comprises the CHP product. Chu's disclosure of pH is irrelevant to the claimed invention not because such pH applies in a different context, but because it describes a completely different ***substance***, a reaction medium, not a pharmaceutical composition comprising CHP and other components, as claimed.

Given that Chu utterly fails to teach or suggest pH of its anhydrous dicalcium phosphate, the skilled artisan has no reasonable expectation that Chu's CHP product will possess a given pH. Even if it is assumed, *arguendo*, that Chu does somehow suggest a pH of its CHP product, there still remains no reasonable expectation that a ***composition*** comprising Chu's CHP product together with an active agent and other excipients would have a pH of 5.0 to 6.0, as recited in the rejected claims.

Apparently responsive to these considerations, the Action highlighted teaching in Appellant's ***own specification*** that pH of a composition can be adjusted by selection of excipients, such as dicalcium phosphate, which can be acidic or neutral, depending on the particular species of dicalcium phosphate and how it is processed during manufacture.[6] Yet, this is a legal red herring that cannot support an obviousness rejection, which must be based on the teachings of the ***prior art***.

Indeed, what is relevant here is that none of the ***cited prior art references***, such as Chu, gives the skilled artisan a reason ***why*** to adjust pH of dicalcium phosphate, teaches ***how*** to adjust pH, or indicates ***what*** pH might pertain to a ***composition*** that contains dicalcium phosphate of a given pH. Simply put, no combination of the cited prior art teaches or suggests a ***composition*** having pH within the range 5.0 to 6.0, as claimed. Accordingly, there is not even a *prima facie* cases of obviousness.

The rejection devolves essentially to the fact-starved allegations that (i) Chu teaches pH of dicalcium phosphate (which it does not), and (ii) pH is an attribute of a pharmaceutical composition

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[5] *See* Chu at col. 1, line 64 to col. 2, line 8 and at col. 3, lines 42-48.

[6] Final Office Action, page 4

comprising the dicalcium phosphate. Because both allegations get nowhere near the claimed invention without factual and legal errors to bridge the gap, the rejection is improper and should be withdrawn.

II. The Cited Prior Art Does Not Suggest a Composition that Inherently Possesses a pH of 5.0 to 6.0

The rejection also manifests legal error by veiling a doctrine of inherency[7] in concluding that prior art "ingredients," when combined, would "reasonably be considered to have similar pH values [as the claimed composition] unless otherwise proven."[8] The Action's reasoning, in essence, arrives at precisely the same point from which it departs: since a known composition possesses certain properties, *ipso facto*, then no such property can be unexpected for purposes of a section 103 analysis.

Yet, by the Action's own admission, the claimed composition is ***not*** known, *per se*, but rather at best would have been obvious from the combined teachings of Pathak, Benneker, and Chu. The factual and legal errors surrounding this assertion are outlined above. Given the ***fact*** that ***none*** of the cited references hint at pH of any "ingredient," much less of the composition as a whole (as claimed), there is no factual basis for the assertion that a ***hypothetical*** composition that might be made by selecting and combining different components from the cited references would possess a pH within the range of 5.0 to 6.0 as claimed. The pH of CHP is not fixed, but instead varies according to its method of manufacture. Hence, a ***composition*** that comprises CHP does not necessarily possess the presently recited pH of 5.0 to 6.0. The Action therefore errs by relying upon inherency in this context.

Indeed, the specification sets forth countervailing evidence that rebuts a rejection based on inherency by showing that any putative prior art composition does not "***necessarily*** possess the characteristics of the claimed product."[9] The application presents in some detail that commercially available CHP is "generally alkaline; i.e. pH ***greater than 7***. . ."[10] For instance, the product DI-TAB has a pH of about 7.4.[11] Yet, some CHP gives rise to acidic or neutral pH, which depends on the form and

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[7] The Action does not actually invoke the term "inherency", *per se*, but it does cite to MPEP § 2112.01 [R-3], which explicitly elaborates upon the doctrine of inherency in anticipation and obviousness rejections. Final Office Action, page 4.

[8] Final Office Action, page 3

[9] *In re Best*, 562 F.2d 1252, 1255 (CCPA 1977).

[10] Specification, page 7 (emphasis added)

[11] *Id.*

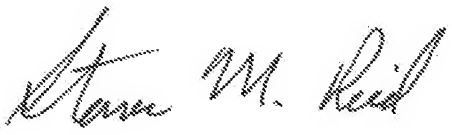
grade of CHP and whether and to what extent impurities remain in the CHP after processing.[12] Still, CHP is generally acknowledged to have a pH of about 7.3.[13]

The pH of a ***composition*** can be governed by a ***blend*** of CHP products, each having their different respective pH values, and by ***excipients other than CHP***.[14] Accordingly, the skilled artisan cannot know *a priori* the pH of a given CHP-containing composition. Because Chu does not teach the pH of its anhydrous dicalcium phosphate, there is no basis for the assertion that pH of Chu's CHP and, allegedly, the pH of a composition comprising that CHP, falls within the claimed range of 5.0 to 6.0. To the extent that the skilled artisan might attribute a particular pH to the CHP taught by Chu, it likely would be a basic pH (e.g., greater than 7), as taught in the application for most CHP. Thus, there is absolutely no basis for the Action's conclusion that Chu could be understood to directly or inherently suggest the pH of the claimed compositions.

For all of these reasons, the cited combination of Benneker, Pathak, and Chu fails to render obvious the claimed composition. Accordingly, Appellants respectfully urge withdrawal of the rejection.

Respectfully submitted,

Date August 6, 2010

By 

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[12] Specification, pages 7-8

[13] Specification, page 8

[14] *Id.*